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(54) Title: MODULATION OF IgG BINDING TO FcRn

(57) Abstract

Disclosed are mutant IgG molecules having altered amino acid sequences in the FcRn–binding region. These changes confere increased or decreased affinity for FcRn and thus, respectively, a decreased or increased rate of clearance from the systemic circulation. Such molecules can be attached to detectable labels or cytotoxic moieties for imaging tissues or for delivering cytotoxins. Also disclosed is a method for identifying IgG molecules with altered half–lives in circulation by contacting the molecules with FcRn.

These studies use mice

mouse

mIgG1	248 * 257 Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Thr Leu Val	(SEQ ID NO: 1)
mIgG1	308 * * 314 Ile Met His Gln Asp Trp Leu	(SEQ ID NO: 2)
mIgG1	429 * * 436 His Glu Gly Leu His Asn His His	(SEQ ID NO: 3)
mIgG2a	248 257 Lys Asp Val Leu Met Ile Ser Leu Ser Pro Asn	(SEQ ID NO: 4)
mIgG2a	308 314 Ile Gln His Gln Asp Trp Met	(SEQ ID NO: 5)
mIgG2a	429 436 His Glu Gly Leu His Asn His Leu Val His	(SEQ ID NO: 6)
mIgG2b	248 257 Lys Asp Val Leu Met Ile Ser Leu Thr Pro Ser	(SEQ ID NO: 7)
mIgG2b	308 314 Ile Gln His Gln Asp Trp Met	(SEQ ID NO: 8)
mIgG2b	429 436 His Glu Gly Leu Lys Asn Tyr Tyr	(SEQ ID NO: 9)
mIgG3	248 257 Lys Asp Ala Leu Met Ile Ser Leu Thr Pro	(SEQ ID NO: 10)
mIgG3	308 314 Ile Gln His Gln Asp Trp Met	(SEQ ID NO: 11)
mIgG3	429 436 His Glu Ala Leu His Asn His His	(SEQ ID NO: 12)

FIG. 2A